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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,792	04/13/2001	Robert F. Margolskee	34116/1051	8395

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EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	PAPER NUMBER
1649	
MAIL DATE	DELIVERY MODE
08/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/834,792	MARGOLSKEE ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *040607*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth on 4/6/2007, have been entered in full.

Response to Amendment

Applicant is notified that any outstanding objection or rejection that is not expressly maintained in this Office action has been withdrawn in view of Applicant's amendments.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims require a method for identifying a compound that induces the perception of bitter taste, however the methods lack essential steps to accomplish the stated goal. The specification apparently mischaracterizes the functional activity of TRP8. It is assumed that the functional experimentation provided in Example 6.2.5 of the specification utilizes mouse TRP8 (trpm5) and not the claimed human TRP8 of SEQ ID NO: 4. In this example, the specification asserts that TRP8 is a store operated Ca^{2+} channel whose function requires external Ca^{2+} and can

be induced through store depletion of Ca^{2+} using thapsigarin. These results appear to be published in Perez-CA et al., Nature Neuroscience 5(11)1169-1176, 2002. However, the art regarding the activity of TRP8 (TRPM5) was, and is, controversial and contradictory to the conclusions presented in Perez and in the instant specification, see Liu and Liman, PNAS 100(15160-15160)2003 , bottom of col. 1 of 15164. Regarding Applicant's published work (Perez, supra) Liu and Liman state that "the conductance described in this report [that of Perez] does not resemble the TRPM5 currents that we recorded, either in rectification properties, Ca^{2+} permeability or sensitivity to La^{3+} block". Furthermore, we were unable to observe significant activation of TRPM5 by short-term thapsigargin treatment" see the top of col 1 of page 15164 and supplemental Figure 7 wherein robust currents are observed after the addition of a Ca^{2+}ionophore and no activity is observed after the addition of thapsigargin. Additionally, Prawitt-D et al., PNAS 100(25)15166-15171, 2003 find no evidence for a store-operated Ca^{2+} activation mechanism for TRPM5 and report that that TRPM5 is essentially impermeable to Ca^{2+}, see col 1 bridging col 2 of page 15166. Likewise, Hofmann et al., Current Biology, 13(1153-1158)2003 report that TRPM5 is a monovalent selective cation channel and not a Ca^{2+} channel, see the Abstract.

The claims have been amended to specify that the level of TRP8 activation is measured by measuring the membrane potential of the cell. Thus, strictly speaking, one would not need to know the correct conductance properties and characteristics of TRP8 to determine whether or not a compound altered the membrane potential of a cell expressing TRP8 if the assays were conducted using an appropriate control cell type that did not express TRP8. The only assays contemplated using the claimed human TRP8 would be those expressing a recombinant TRP8 in

host cells, e.g. as those in the Examples. However, the claims do not recite any method step(s) wherein the activity of cells expressing the TRP8 are compared to the activity of similar cells not expressing TRP8. Thus, having followed the method steps of the claims, the skilled artisan would have no idea whether a compound that altered the membrane potential of a cell expressing the TRP8 had done so in anyway that had anything to do with the TRP8 protein, nor less so about taste in general and even less regarding bitter taste. The activity could be due to any number of mechanisms peculiar to the host cell, e.g. a frog egg as in the Examples, and need not be related to TRP8 or taste. Thus, the skilled artisan practicing the method steps would not have accomplished the recited goal of the claims.

Second, the Trp8 channel (a.k.a hTrpm5) is stated in the specification to be involved in both bitter and sweet taste perception (e.g. the abstract); additionally it is known in the art to be involved in bitter, sweet, and amino acid taste perception (e.g. see the Discussion on page 5783 of Zhang-Z et al. J. Neuroscience 27(5777-5786)2007). The claims lack a step or steps to follow to accomplish the goal of identifying a compound that induces perception of bitter taste. Thus, the skilled artisan practicing the method steps would not have accomplished the recited goal of the claims. In reply to the instant rejection, Applicant is cautioned against the introduction of new matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims require a method for identifying a compound that induces the perception of bitter taste, however the methods lack essential steps to accomplish the stated goal. As set forth above, the claims lack the essential steps of determining whether any activity of a compound on membrane potential had any effect on the TRP8 protein and thus might be relevant to taste, and nor any steps to determine if any effect on TRP8 translates to an effect on bitter taste. Thus, the claims do not set forth a step or steps for the artisan to follow which lead back to and accomplish the recited goal. The claims are therefore indefinite as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 9:00 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (571) 272-0841. Official papers filed by fax should be directed to **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

August 12, 2007

LORRAINE SPECTOR
PRIMARY EXAMINER